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Structure Determination of the Salmonella Typhimurium Quorum Sensor Protein

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Introduction: This research investigates the biochemical nature of cell-cell communication in bacteria. Bacteria monitor their local population density through the exchange of small extracellular signaling molecules called autoinducers. This communication, known as quorum sensing, allows bacteria to coordinate gene expression as a population, regulating such processes as bioluminescence, virulence factor expression, antibiotic expression, and biofilm development. One signaling molecule, autoinducer-2 (AI-2), has been shown to be produced by a large number of bacterial species, and has been proposed to be a 'universal' signal for interspecies communication. The structure of the primary AI-2 receptor in *Vibrio harveyi*, LuxP, in complex with AI-2 was recently determined in our laboratory. The chemical identity of AI-2 was determined through interpretation of the high resolution electron density map of the complex. This LuxP-AI-2 complex is believed to interact with LuxQ, a sensor kinase, to transduce the autoinducer signal.

Here, we seek to determine the high resolution structure of LsrB, the *Salmonella typhimurium* homologue of LuxP, in complex with its autoinducer ligand. Though it has low sequence homology to LuxP, LsrB has been shown to bind to an autoinducer molecule which stimulates responses such as bioluminescence when assayed with *Vibrio harveyi*, though ^{11}B NMR data suggests chemical rearrangement of the autoinducer. The structure will provide high resolution details of the LsrB binding site and the bound autoinducer, and will also be of great use in the design of molecules, both agonists and antagonists, which can bind to LsrB and other quorum sensing receptors. We plan to undertake synthesis and structural studies of such molecules, which may provide leads for the development of antibiotic drugs that target quorum sensing.